



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
---------------	-------------	-----------------------	---------------------

577494.804 03/14/90 LONG

RICHARD E. FICHTER  
BACON & THOMAS  
625 SLATERS LANE  
FOURTH FLOOR  
ALEXANDRIA, VA 22314

GARDNER, D

APR 1991 PAGE NUMBER

125  
DATE MAILED:

06/03/91

### NOTICE OF ALLOWABILITY

#### PART I

1. ☒ This communication is responsive to papers filed on May 10, 1991
2. ☒ All the claims being allowable. PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice Of Allowance And Issue Fee Due or other appropriate communication will be sent in due course.
3. ☒ The allowed claims are 1-3, 5-7, 12-17; now 1-3, 4-6, 7, 11, 12, 8, 9, 10
4. ☐ The drawings filed on \_\_\_\_\_ are acceptable.
5. ☒ Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received. ☐ not been received. ☒ been filed in parent application Serial No. 07/131442, filed on 2-11-87
6. ☒ Note the attached Examiner's Amendment.
7. ☐ Note the attached Examiner Interview Summary Record, PTOL-413.
8. ☐ Note the attached Examiner's Statement of Reasons for Allowance.
9. ☐ Note the attached NOTICE OF REFERENCES CITED, PTO-892.
10. ☐ Note the attached INFORMATION DISCLOSURE CITATION, PTO-1449.

#### PART II

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" indicated on this form. Failure to timely comply will result in the ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

1. ☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.
2. ☐ APPLICANT MUST MAKE THE DRAWING CHANGES INDICATED BELOW IN THE MANNER SET FORTH ON THE REVERSE SIDE OF THIS PAPER.
  - a. ☐ Drawing Informalities are indicated on the NOTICE RE PATENT DRAWINGS, PTO-846, attached hereto or to Paper No. \_\_\_\_\_ CORRECTION IS REQUIRED.
  - b. ☐ The proposed drawing correction filed on \_\_\_\_\_ has been approved by the examiner. CORRECTION IS REQUIRED.
  - c. ☐ Approved drawing corrections are described by the examiner in the attached EXAMINER'S AMENDMENT. CORRECTION IS REQUIRED.
  - d. ☐ Formal drawings are now REQUIRED.

Any response to this letter should include in the upper right hand corner, the following information from the NOTICE OF ALLOWANCE AND ISSUE FEE DUE: ISSUE BATCH NUMBER, DATE OF THE NOTICE OF ALLOWANCE, AND SERIAL NUMBER.

#### Attachments:

- ☒ Examiner's Amendment
- Examiner Interview Summary Record, PTOL-413
- Reasons for Allowance
- Notice of References Cited, PTO-892
- Information Disclosure Citation, PTO-1449
- Notice of Informal Application, PTO-152
- Notice re Patent Drawings, PTO-846
- Listing of Bonded Draftsmen
- Other

*Frederick E. Waddell*  
Frederick E. Waddell  
Supervisory Patent Examiner  
Group 120

Serial No. 07/494804

-2-

Art Unit 125

An Examiner's Amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. § 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the Issue Fee.

Claim 1 is amended as follows:

2. ~~1.~~ (Twice amended) A pharmaceutical composition which is an aqueous formulation for oral administration of an effective amount of ranitidine and/or one or more physiologically acceptable salts thereof, said formulation comprising a stabilizing effective amount of ethanol and said composition having a pH in the range of 6.5-7.5.

Any inquiry concerning this communication should be directed to Diane Gardner at telephone number (703) 308-4610.

  
Frederick E. Waddell  
Supervisory Patent Examiner  
Group 120

Gardner:dlg  
May 30, 1991

97

G 000213


**UNITED STATES DEPARTMENT OF COMMERCE**  
**Patent and Trademark Office**

 Address: Box ISSUE FEE  
 COMMISSIONER OF PATENTS AND TRADEMARKS  
 Washington, D.C. 20231

 RICHARD E. FICHTER  
 BADON & THOMAS  
 625 SLATERS LANE  
 FOURTH FLOOR  
 ALEXANDRIA, VA 22314

**NOTICE OF ALLOWANCE  
 AND ISSUE FEE DUE**

APP. NO.	FILED DATE	TOTAL CLAIMS	EXAMINER AND GROUP	DATE			
07/494,804	03/14/90	012	GARDNER, D.	125 06/03/91			
LONG,			DAVID R.				
AQUEOUS RANITIDINE COMPOSITIONS STABILIZED WITH ETHANOL (AS AMENDED)							
APP. NO.	CLASS	SUBCLASS	BATCH NO.	APP. TYPE	SMALL ENTITY	FEE DUE	DATE
1	514	471.000	009	UTILITY	NO	\$1050.00	09/03/91

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT.  
 PROSECUTION ON THE MERITS IS CLOSED.**

**THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS  
 APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.**

**HOW TO RESPOND TO THIS NOTICE:**

I. Review the SMALL ENTITY Status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

- A. If the Status is changed, pay twice the amount of the FEE DUE shown above and notify the Patent and Trademark Office of the change in status, or
- B. If the Status is the same, pay the FEE DUE shown above.

If the SMALL ENTITY is shown as NO:

- A. Pay FEE DUE shown above, or
- B. File verified statement of Small Entity Status before, or with, payment of 1/2 the FEE DUE shown above.

II. Part B of this notice should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by a charge to deposit account, Part B should be completed and returned. If you are charging the ISSUE FEE to your deposit account, Part C of this notice should also be completed and returned.

III. All communications regarding this application must give series code (or filing date), serial number and batch number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER: Patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees.**

- 4 -

CLAIMS

1. A pharmaceutical composition which is an aqueous formulation of ranitidine and/or one or more physiologically acceptable salts thereof, said formulation also containing ethanol.
2. A pharmaceutical composition according to claim 1 containing 2.5% to 10% weight/volume ethanol based on the complete formulation.
3. A pharmaceutical composition according to claim 1 containing 7% to 8% weight/volume ethanol based on the complete formulation.
4. A pharmaceutical composition according to claim 1 having a pH in the range 6.5 to 7.5.
5. A pharmaceutical composition according to claim 1 having a pH in the range 6.8 to 7.4.
6. A pharmaceutical composition according to claim 1 having a pH in the range 7.0 to 7.3.
7. A pharmaceutical composition according to claim 1 wherein said pH is obtained by the use of buffer salts.
8. A pharmaceutical composition as claimed in claim 1 suitable for oral administration.
9. A pharmaceutical composition as claimed in claim 8 containing 20-400 mg ranitidine per 10 ml dose expressed as free base.
10. A pharmaceutical composition according to claim 8 containing 20-200 mg ranitidine per 10 ml dose expressed as free base.

G 000243

- 5 -

11. A pharmaceutical composition according to claim 8  
containing 150 mg ranitidine per 10 ml dose expressed as  
5 free base.

12. A pharmaceutical composition according to claim 1  
prepared using ranitidine in the form of the  
hydrochloride salt.

10

13. A pharmaceutical composition which is an aqueous  
formulation of ranitidine suitable for oral  
administration containing 150 mg ranitidine per 10 ml  
dose expressed as free base, said formulation having a  
15 pH in the range 7.0 to 7.3 and also containing 7% to 8%  
weight/volume ethanol based on the complete formulation.

14. A pharmaceutical composition according to claim 13  
wherein said pH is obtained by the use of buffer salts.

G 000244



12X  
2-13-88  
STO 30  
G-125

RECEIVED

MAR 14 1988

GROUP 120

#2  
JRP  
4/4/88

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

David Richard LONG

Serial No. 131,442

Filed: December 11, 1987

For: PHARMACEUTICAL COMPOSITIONS

Group Art Unit: 123

S. FRIEDMAN

COMPLETION OF CLAIM FOR PRIORITY

Hon. Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

Attached hereto is a certified copy of UK Application No. GB 8629781,  
dated December 12, 1986, to complete the claim for priority made in the  
Declaration of the above-identified application.

Respectfully submitted,

*Richard E. Fichter*  
Richard E. Fichter  
Reg. No. 26,382

BACON & THOMAS  
625 Slaters Lane, Fourth Floor  
Alexandria, VA 22314

(703) 683-0500

Date: March 11, 1988  
/bjr

12

G 000249



THE PATENT OFFICE  
STATE HOUSE  
66-71 HIGH HOLBORN  
LONDON WC1R 4TP

RECEIVED

MAR 14 1988

*Cut by  
Certification Branch GROUP 120*

I, the undersigned, being an officer duly authorised in accordance with Section 62(3) of the Patents and Designs Act 1907, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents, has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or the inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Please turn over

M1181

*12  
11*

G 000250

**G 000251**



## PATENTS ACT 1977

PATENTS FORM No. 1/77 (Revised 1982)  
(Rules 16, 19)

12 DEC 1986

The Comptroller  
The Patent Office1986  
29781REQUEST FOR GRANT OF A PATENT  
8629781

THE GRANT OF A PATENT IS REQUESTED BY THE UNDERSIGNED ON THE BASIS OF THE PRESENT APPLICATION

I Applicant's or Agent's Reference (Please insert if available) HA107

II Title of Invention PHARMACEUTICAL COMPOSITIONS

III Applicant or Applicants (See note 2)

Name (First or only applicant) Glaxo Group Limited

Country United Kingdom State ADP Code No.

Address Clarges House, 6-12 Clarges Street, London W1Y 8DH, England.

Name (of second applicant, if more than one)

Country State

Address

IV Inventor (see note 3)

(b) A statement on Patents Form No 7/77 will be  
furnished

V Name of Agent (if any) (See note 4) ELKINGTON AND FIFE ADP CODE NO

VI Address for Service (See note 5) High Holborn House  
52/54 High Holborn  
London WC1V 6SH

VII Declaration of Priority (See note 6)

Country

Filing date

File number

VIII The Application claims an earlier date under Section 8(3), 12(6), 15(4), or 37(4) (See note 7)

Earlier application or patent number

and filing date

G 000252

## IX Check List (To be filled in by applicant or agent)

- |  |  |
|--|--|
| A The application contains the following number of sheet(s): | B The application is made in accordance with |
| 1 Request 1 Sheet(s):  | 1 Priority document                          |
| 2 Description 4 Sheet(s):                                    | 2 Translation of priority document           |
| 3 Claim(s) Sheet(s):   | 3 Request for Search                         |
| 4 Drawing(s) Sheet(s):                                       | 4 Statement of Invention and Right to Grant  |
| 5 Abstract Sheet(s):   |  |

X It is suggested that Figure No. of the drawings (if any) should accompany the abstract when published.

XI Signature (See note 8)

*E. Chong*  
ELKINGTON AND FEE (CAB/IR)

## NOTES

1. This form, when completed, should be brought or sent to the Patent Office together with the prescribed fees and two copies of the description of the invention, and of any drawings.
2. Enter the name and address of each applicant. Names of individuals should be indicated in full and the surname or family name should be underlined. The names of all partners in a firm must be given in full. Bodies corporate should be designated by their corporate name and the country of incorporation and, where appropriate, the state of incorporation within that country should be entered where provided. Full corporate details, eg "a corporation organised and existing under the laws of the State of Delaware, United States of America," trading styles, eg "trading as xyz company", nationality, and former names, eg "formerly [known as] ABC Ltd." are not required and should not be given. Also enter applicant(s) ADP Code No. (if known).
3. Where the applicant or applicants is/are the sole inventor or the joint inventors, the declaration (a) to that effect at IV should be completed, and the alternative statement (b) deleted. If, however, this is not the case the declaration (a) should be struck out and a statement will then be required to be filed upon Patent Form No 7/77.
4. If the applicant has appointed an agent to act on his behalf, the agent's name and the address of his place of business should be indicated in the spaces available at V and VI. Also insert agent's ADP Code No. (if known) in the box provided.
5. An address for service in the United Kingdom to which all documents may be sent must be stated at VI. It is recommended that a telephone number be provided if an agent is not appointed.
6. The declaration of priority at VII should state the date of the previous filing and the country in which it was made and indicate the file number, if available.
7. When an application is made by virtue of section 8(3), 12(8), 15(4) the appropriate section should be identified at VIII and the number of the earlier application or any patent granted thereon identified.
8. Attention is directed to rules 90 and 106 of the Patent Rules 1982.
9. Attention of applicants is drawn to the desirability of avoiding publication of inventions relating to any article, material or device intended or adapted for use in war (Official Secrets Acts, 1911 and 1920). In addition after an application for a patent has been filed at the Patent Office the comptroller will consider whether publication or communication of the invention should be prohibited or restricted under section 22 of the Act and will inform the applicant if such prohibition is necessary.
10. Applicants resident in the United Kingdom are also reminded that, under the provisions of section 23 applications may not be filed abroad without written permission or unless an application has been filed not less than six weeks previously in the United Kingdom for a patent for the same invention and no direction prohibiting publication or communication has been given or any such direction has been received.

17/13  
G 000253

PHARMACEUTICAL COMPOSITIONS

The present invention relates to a pharmaceutical composition containing as active ingredient the histamine  $H_2$  antagonist ranitidine.

Ranitidine,  $[N-[2-[[[5-(dimethylamino)methyl-2-furanyl]methyl]-thio]ethyl]-N'-methyl-2-nitro-1,1-ethenediamine]$ , and its physiologically acceptable salts are described in British Patent Specification No. 1565966. In that specification there is reference to liquid formulations for oral and parenteral administrations and there is a description of an aqueous based formulation for intravenous use and another of an oral syrup. Both of these formulations contained sufficient hydrochloric acid to achieve a pH of 5.0 and the syrups also contained Sorbitol solution BPC and a flavour as required.

British Patent Application No. GB 2142820A describes aqueous based formulations containing ranitidine and/or one or more of its physiologically acceptable salts thereof having a pH within the range 6.5-7.5. In that specification there is reference to liquid formulations for oral and parenteral administration and there are examples of aqueous formulations for intravenous and oral use. These formulations contain ranitidine hydrochloride and are buffered to a pH of approximately 7 and for intravenous administration the formulations also contain phenol or sodium chloride. For oral administration the formulation also contains hydroxypropylmethyl cellulose as a viscosity enhancing agent, a preservative (parabens), a sweetening agent and a flavour. These compositions have a significantly greater shelf-life over those in British Patent No. 1565966.

15 OVER  
14

- 2 -

We have now surprisingly found that the stability of ranitidine in aqueous based formulations and more particularly aqueous based formulations for oral administration may be substantially enhanced by the addition of ethanol to the formulation.

5 Thus the present invention provides a pharmaceutical composition which is an aqueous formulation of ranitidine and/or one or more physiologically acceptable salts thereof also containing ethanol. The aqueous formulation is prepared using ingredients of a purity such that it is suitable for administration to patients and will in general  
10 contain at least one conventional pharmaceutical excipient in addition to the ethanol and ranitidine and/or physiologically acceptable salts thereof.

The amount of ethanol present in the formulation is such that the resulting formulation has the enhanced stability. Preferably the  
15 amount of ethanol in the composition on a weight/volume basis of the complete formulation, is within the range 2.5% to 10%, and more particularly is between 5 to 10% w/v, more especially 7-8% w/v.

Preferred compositions according to the invention are those in which the pH of the aqueous formulation is within the range 6.5 to  
20 7.5, particularly 6.8 to 7.4 and more especially 7 to 7.3. The required pH of the formulation is preferably obtained by the use of suitable buffer salts for example, potassium dihydrogen orthophosphate, and disodium hydrogen orthophosphate or citric acid and disodium hydrogen orthophosphate.

25 A preferred embodiment of the invention is an aqueous formulation for oral administration. Such a formulation may comprise ranitidine and/or one or more of its physiologically acceptable salts dissolved in water, ethanol, a preservative and a viscosity enhancing agent. Preferably the required pH of the formulation is obtained by  
30 the use of appropriate buffer salts. Optionally the composition may

7/10 15  
G 000255

- 3 -

also contain other conventional excipients such as a sweetener, a flavour and/or flavouring aids.

Examples of suitable preservatives include one or more alkyl hydroxybenzoates such as methyl, ethyl, propyl and/or butyl hydroxybenzoates.

Examples of suitable viscosity enhancing agents include Xanthan gum, sorbitol glycerol, sucrose or a cellulose derivative such as carboxymethylcellulose or a salt thereof of a C<sub>1-4</sub> alkyl and/or a hydroxy-C<sub>2-4</sub>alkyl ether of cellulose such as methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxyethylmethylcellulose and hydroxypropylmethylcellulose.

Examples of suitable sweeteners include saccharin sodium, sodium cyclamate, sorbitol and sucrose.

Examples of suitable flavouring agents include 'mint' flavours such as peppermint flavouring agents.

The concentration of ranitidine in the oral formulation, expressed as free base, is conveniently within the range 20-400mg per 10ml, for example 20-200 mg per 10ml, more particularly 150mg per 10ml dose.

The amount of ethanol in the formulation for oral administration, expressed as a percentage of the complete formulation on a weight/volume basis, is preferably within the range 2.5 to 10%, and more particularly between 5 to 10%, more especially 7-8%.

The amount of viscosity enhancing agent in the formulation will preferably be sufficient to give a solution with a viscosity in the range of 10 to 100 centipoises.

The aqueous formulations for oral administration are

14  
Oler

G 000256

- 4 -

conveniently prepared by mixing an aqueous solution of ranitidine and/or one or more of its physiologically acceptable salts together with ethanol and the excipients, with aqueous solution or dispersion of the viscosity enhancing agent.

5 The aqueous formulations according to the invention are preferably prepared using ranitidine in the form of its hydrochloride salt.

An illustrative example of a formulation according to the invention is as follows. In this example the relative proportions of ranitidine hydrochloride and the buffer salts are such that the  
10 formulation has a pH of approximately 7.

Ranitidine oral liquid formulation (150mg/10ml) expressed as free base

15

	% w/v
Ranitidine hydrochloride	1.68
Ethanol	7.5
20 Potassium dihydrogen orthophosphate	0.095
Disodium hydrogen orthophosphate anhydrous	0.350
Hydroxypropylmethylcellulose	qs
Preservative	qs
Sweetening agents	qs
25 Flavour	qs
Purified water BP to	100ml

G 000257

RECEIVED  
APR 23 1987  
#3  
381  
421  
FSC  
APR  
SRC  
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
GROUP 100

In re Application of:

David R. LONG

Serial No. 131,442

Filed: December 11, 1987

For: PHARMACEUTICAL COMPOSITIONS

Group Art Unit: 123  
S. Freeman

INFORMATION DISCLOSURE STATEMENT

Honorable Commissioner of Patents  
and Trademarks  
Washington, D.C. 20231

Sir:

Prior to an examination of the merits of the above identified application, the attention of the Examiner is directed to the following information, which may be considered material to the prosecution of the present application. The attached Form PTO-1449 lists the publications, and a copy of each U.S. patent is submitted herewith.

The most relevant publications of which Applicant is aware are British Patent Specification No. 1,565,966 and British Patent Specification No. 2,142,820A. The specifications are discussed at Applicant's specification page I, lines 4-25. The U.S. equivalents of these publications are U.S. Patent Nos. 4,128,658 and 4,585,790.

U.S. Patent No. 4,585,790 refers to a publication by Padfield et al ("The Chemical Use of Ranitidine," Medicine Publishing Foundation Symposium Series 5, Oxford, Medicine Publishing Foundation 1982 pages 18-22). This publication refers to an aqueous formulation of ranitidine hydrochloride at its natural pH, i.e., about 5.5. This publication is not believed to be as relevant as the publications discussed in Applicant's specification. The Examiner is requested to contact the undersigned if

19/16

G 000258

Serial No. 131,442

a copy of this publication is required.

In view of the above comments and information disclosure,  
an early action on the merits of this application is now believed to be  
in order and is most respectfully requested.

Respectfully submitted,

*Richard E. Fichter*  
Richard E. Fichter  
Registration No. 26,382

BACON & THOMAS  
625 Slaters Lane  
Fourth Floor  
Alexandria, Virginia 22314  
Phone: (703) 683-0500

April 8, 1988

20 19



[illegible]


**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

 Address COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
07/131,442	12/11/87	LONG	D REFJIM5557

BACON & THOMAS  
625 SLATERS LANE - 4TH FLOOR  
ALEXANDRIA, VA 22314

EXAMINER	
FRIEDMAN, S	
ART UNIT	PAPER NUMBER
125	4

DATE MAILED:

05/05/88

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

- ☒ This application has been examined ☐ Responsive to communication filed on \_\_\_\_\_ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.  
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

- |   |   |
|---|---|
| 1. <input checked="" type="checkbox"/> Notice of References Cited by Examiner, PTO-492. | 2. <input type="checkbox"/> Notice re Patent Drawing, PTO-946.                  |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449                  | 4. <input type="checkbox"/> Notice of Informal Patent Application, Form PTO-152 |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474      | 6. <input type="checkbox"/> _____   |

**Part II SUMMARY OF ACTION**

1. ☒ Claims 1-14 are pending in the application.  
Of the above, claims \_\_\_\_\_ are withdrawn from consideration.
2. ☐ Claims \_\_\_\_\_ have been cancelled.
3. ☐ Claims \_\_\_\_\_ are allowed.
4. ☒ Claims 1-14 are rejected.
5. ☐ Claims \_\_\_\_\_ are objected to.
6. ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings which are acceptable for examination purposes until such time as allowable subject matter is indicated.
8. ☐ Allowable subject matter having been indicated, formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on \_\_\_\_\_. These drawings are ☐ acceptable; ☐ not acceptable (see explanation).
10. ☐ The ☐ proposed drawing correction and/or the ☐ proposed additional or substitute sheet(s) of drawings, filed on \_\_\_\_\_ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed \_\_\_\_\_, has been ☐ approved. ☐ disapproved (see explanation). However, the Patent and Trademark Office no longer makes drawing changes. It is now applicant's responsibility to ensure that the drawings are corrected. Corrections **MUST** be effected in accordance with the instructions set forth on the attached letter "INFORMATION ON HOW TO EFFECT DRAWING CHANGES", PTO-1474.
12. ☒ Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☒ been received ☐ not been received. ☐ been filed in parent application, serial no. \_\_\_\_\_; filed on \_\_\_\_\_.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

23  
22

PTOL-324 (Rev. 7-82)

EXAMINER'S ACTION

G 000263

Serial No. 131,442

-2-

Art Unit 125

Claim 1-10 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

"Also containing ethanol" (claim 1) is indefinite as to what else is included. All claims should show how the ~~it~~ is arrived at.

Claim 1-12 rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited in accordance with the entire disclosure. See MPEP 706.03(n) and 706.03(z).

All claims should recite amounts for all ingredients. Claims failing to do such are broader than unwanted.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claim 1-14 rejected under 35 U.S.C. 103 as being unpatentable over Chemical Abstracts, both.

24  
23

G 000264

Serial No. 131,442

-3-

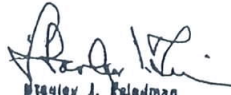
Art Unit 125

The art teaches the combining of ranitidine and an alcohol; e.g. ethanol. The addition of a non-critical pH limit and non-critical amounts are not seen as patentable limitations to the various claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Friedman whose telephone number is (703) 557-9592.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 557-3920.

4-29-88;df

  
Gregory J. Friedman  
Primary Examiner  
Group Art Unit 125

25  
24

G 000265



In re Application Serial No. 131,442

Applicant: LONG

Group Art Unit: 125

Filing Date: December 11, 1988

Examiner: Friedman

For: PHARMACEUTICAL COMPOSITIONS

REC-100  
18 JUL 73  
0000000000

AMENDMENT

Honorable Commissioner of Patents  
and Trademarks  
Washington, D.C. 20231

**SIR:**

This is in response to the Official Action of May 5, 1988 in connection with the above-identified application. The period for response to this Official Action has been extended to expire on November 5, 1988 by the filing herewith of a Petition for three month Extension of Time and payment of the required fee. Please amend the above-identified application as follows:

IN THE CLAIMS

Please amend Claim 1 as follows:

1. (Amended) A pharmaceutical composition which is an aqueous formulation of ranitidine and/or one or more physiologically acceptable salts thereof, said formulation also containing a stabilizing effect amount of ethanol and said composition having a pH in the range of 6.5 to 7.5.

Please cancel Claim 4 without prejudice or disclaimer.

## REMARKS

Applicant has amended the claims in order to more particularly define the invention. Claims 1 and 4 have been combined and the amount ethanol present has been functionally defined. Claim 4 has been cancelled from the application. The claims remaining in the application are Claims 1-3 and 5-10. Applicant

~~21~~  
26

**G-000267**

most respectfully submits that all the claims now present in the application are in full compliance with 35 USC 112 and are clearly patentable over the references of record.

The rejection of Claims 1-10 under 35 USC 112 second paragraph as being indefinite has been carefully considered. The expression "also containing ethanol" has been modified to specify that the amount of ethanol contained in the composition is a stabilizing amount of ethanol and this amendment is fully supported by applicant's specification, at page 2, lines 4 and 5.

In addition, the pH range from Claim 4 has been included in Claim 1. Applicant most respectfully submits that there is no requirement that the method of obtaining the pH be set forth in the claims. This would be fully appreciated by one of ordinary skill in the art. In fact, the desired pH can be simply achieved by adding an appropriate amount of a physiologically acceptable acid or base to the solution, depending on whether the solution is prepared from ranitidine free base or an acid addition salt thereof. It is not necessary to use buffer salts to obtain the desired pH, although it may often be more convenient to do so. Accordingly, it can be seen that the means for adjusting pH are entirely conventional and therefore, it is most respectfully requested that this aspect of the rejection under 35 USC 112 be withdrawn. As far as Claim 7 is concerned, having inserted the pH range in Claim 1, the amount of buffer salts is thereby predetermined, depending on the specific buffer salts that are used.

The rejections of Claims 1-14 under 35 USC 103 as being unpatentable over Chemical Abstracts has been carefully considered. In the Official Action it is urged that the art teaches the cojoining of ranitidine and an alcohol; e.g., ethanol. The addition of a non-critical pH limitation and non-critical amounts are not seen as patentable limitations to the various claims. This rejection having been carefully considered is most respectfully traversed.

At the outset, applicant specifically traversed the statement in the Official Action that the references relied upon by the Examiner teach the cojoining of ranitidine and an alcohol, e.g., ethanol. Applicant most respectfully submits that the art does not teach the cojoining of ranitidine and an alcohol in a pharmaceutical composition. These references do not lead one



of ordinary skill in the art any way to expect that the stability of ranitidine in an aqueous pharmaceutical composition could be enhanced by the presence of ethanol and does not suggest the presence of ethanol in such compositions.

The first Chemical Abstract reference (97 61014G) relates to the Glaxo patent for a new polymorphic form of ranitidine hydrochloride (designated form 2) and includes a description of processes for its production. Applicant most respectfully submits that all that one of ordinary skill in the art can infer from this reference is that ranitidine hydrochloride must be reasonably stable in ethanol since ethanol is used as a solvent for recrystallization. However, there is no teaching whatever that the stability of ranitidine or its salts as a solution in water is enhanced by the presence of ethanol and no suggestion that ethanol should be included in pharmaceutical compositions containing ranitidine as presently claimed.

The second Chemical Abstract reference (104 102280z) relates to a paper in a Scandinavian journal indicating the presence of ethanol in a person's diet did not adversely affect the gastric acid secretion inhibiting properties of ranitidine. Again, there is absolutely no teaching in this reference that would lead one of ordinary skill in the art to expect that ethanol would enhance the stability of ranitidine in aqueous pharmaceutical compositions or would suggest to one of ordinary skill in the art that ethanol should be added to such compositions.

In summary, the prior art relied upon in the rejection is in fact, extremely far removed from the present claimed invention and no way renders it obvious. Accordingly, it is most respectfully requested that this rejection be withdrawn.

Serial No. 131,442

-2-

Art Unit 125

Claims 1-3 and 5-14 remain rejected over Chemical Abstract (both) under 35 USC 103 for the reasons fully and clearly of record.

Chemical Abstract 97 does teach ranitidine in the presence of ethanol (applicant admits same, page 3 response).

The alleged advantages have not been demonstrated for the parameters claimed versus adjacent parameters.

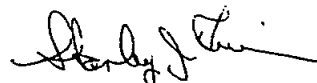
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner S. Friedman whose telephone number is (703) 557-9592.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 557-3920.

11/25/88;rbb



Stanley J. Friedman  
Primary Examiner  
Art Unit 12

32  
31

G 000272